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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/089,678	04/03/2002	Shinichiro Asano	Q68821	5542

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EXAMINER	
ROBINSON, HOPE A	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 06/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/089,678	ASANO ET AL.	
	Examiner	Art Unit	
	Hope A. Robinson	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) *3-5,7,8 and 11* is/are withdrawn from consideration.

5)☒ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6,9 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. PCT/JP01/06660.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election without traverse of Group I (claims 1, 2, 6, 9 and 10) is acknowledged.

2. Claims 3-5, 7-8 and 11 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on April 19, 2004.

3. The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1653.

Specification

4. The specification is objected to because of the following informalities: on page 1 and throughout the specification genus and species names are underlined, however, it is suggested that applicant italicized these names because the underlining is confusing as that is what's used to indicate an insertion of materials via an amendment.

The specification is also objected to because the priority information is not disclosed on page 1, for example, "This application is a 371 of PCT/JP01/06660, filed August 2, 2001 which claims priority to JP 2000-236140 filed August 3, 2000".

Further, the specification is objected to because trademarks are disclosed and they are not capitalized. The use of the trademark such as TRIS-HCL©, has been noted in this application (see page 22). It should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

See also page 2 (lines 8-11) where the following appears, "Furthermore, the spores germinate under nutritional conditions and they invade into the hemocele of the insect according as the vegetative cells propagate, thus causing blood poisoning", which seems to be missing a phrase.

In addition, see page 3 lines 16-17 for "...released together with spores into medium according as the bacterial cell is destructed". Also see page 8, lines 19-20 for "...they have found out a *Bacillus thuringiensis serovar galleriae* SD502...".

The specification is also objected to because the following appears on for example page 9, line 15, " SEQ. ID. No.1" and this notation does not comply with the sequence rules, the sequence notation should be "SEQ ID NO:1".

At pages 9-11 of the specification, the claims are disclosed by number not just content, it is suggested that the numbers are deleted from the instant specification as during prosecution claims can be deleted.

On page 11, line 2, deletion of "a" is needed in the following sentence "...insect and the plant is protected from a damage...".

Compliance with the sequence rules and correction of the above is required.

Abstract

5. The abstract of the disclosure is objected to because:

1) Abstract has two paragraphs, 2)The use of the word "novel" in the abstract is objected to as "novel" is a determination of the office not an assertion by applicant and 3)It is suggested that the run on sentences are broken into smaller units.

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

Correction is required. See MPEP § 608.01(b).

Drawing

6. The Drawings filed on April 3, 2002 are objected to because Figure 1 of an electron micrograph is not clear. Applicant needs to submit formal drawings.

Claim Objection

7. Claims 1-2 and 9-10 are objected to because of the following informalities:

Claims 1-2 are objected to for the recitation of " SEQ. ID. No.1" as this notation does not comply with the sequence rules, the sequence notation should be "SEQ ID NO:1".

For clarity the "a" in claims 9 and 10 should be deleted, where it appears in front of the word "damage".

For clarity item (2-3) should recited "a microbe transformed with a DNA containing a nucleotide sequence encoding a protein having an amino acid sequence described in SEQ ID NO:1 in the Sequence Listing" as in item (1-3) as the mere recitation of "transformed microbe" is insufficient.

Compliance with the sequence rules and correction of the above is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

8. Claims 1-2 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 1-2 are drawn to a protein, which reads on a product of nature. The claims should be amended to indicate the hand of the inventor, for example the insertion of "isolated" or "purified" in connection with the protein to identify a product not found in nature (see MPEP 2105).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-2, 6 and 9-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the protein set forth in SEQ ID NO:1, does not reasonably provide enablement for any variant thereof or an amino acid sequence derived by addition, substitution or deletion of a plurality of amino acids contained in SEQ ID NO:1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. The enablement requirement refers to the requirement that the specification describe how to make and how to use the invention. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to: Quantity of Experimentation Necessary; Amount of direction or guidance presented; Presence or absence of working examples; Nature of the Invention; State of the prior art and Relative skill of those in the art; Predictability or unpredictability of the art and Breadth of the claims. Each factor will be discussed below.

The claimed invention is directed to a protein comprising SEQ ID NO:1 and this protein sequence is recited as being variable (see claim 2). The specification is devoid of any guidance/direction as to what residues in what positions can be substituted, deleted or added. In fact the plurality of variations contemplated could result in a protein that is structurally different, functionally distinct or non-functional, as the claim and instant specification does not teach how to retain function. The instant specification

does not disclose any special attributes or properties of the claimed variant or provide data that is demonstrative of the retention of function following the unlimited variability contemplated. Therefore, while it is known in the art that many amino acid substitutions are possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited, as certain positions in the sequence are critical to the protein's structure/function relationship. It is also known in the art that a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many cases. For example, various sites or regions directly involved in binding activity and in providing the correct three-dimensional spatial orientation of binding and active sites can be affected (see Wells, Biochemistry, vol. 29, pages 85-09-8517, 1990). The instant specification provides no guidance/direction as to which regions of the protein would be tolerant of modifications and which would not, and it provides no working examples of any variant sequence that is encompassed by the claims. It is in no way predictable that randomly selected mutations, such as deletions, substitutions, additions, etc., in the disclosed sequence would result in a protein having activity comparable to the one disclosed. As plural substitutions for example are introduced, their interactions with each other and their effects on the structure and function of the protein is unpredictable.

Additionally, the specification is not considered to be enabling as the starting materials necessary to make the invention is not available. The specification on page 11 state that *Bacillus thuringiensis serovar galleriae* SDS502 strain producing a protein

having SEQ ID NO:1 was deposited at the National Institute of Advanced Industrial Science and Technology, however, the specification does not provide direction/guidance as to whether the deposited materials are publicly available, to enable a skilled artisan to practice the claimed invention.

The working examples provided do not rectify the missing information in the instant specification pertaining to the claimed variant. The nature and properties of this claim is difficult to ascertain from the examples provided as one of skill in the art would have to engage in undue experimentation to construct the variants of the claimed invention and examine the same for function. The specification does not provide support for the broad scope of the claims, which encompass all modifications and any variants thereof of the claimed sequence. Therefore, absent direction/guidance regarding whether the structure can tolerate the modifications contemplated a non-functional protein may result and one of skill in the art would not be able to practice the claimed invention commensurate in scope with the claims. The amino acid sequence of a protein determines its structural and functional properties, and predictability of what mutations can be tolerated in a protein's sequence and result in a certain activity, which is very complex, and well outside the realm of routine experimentation, because accurate predictions of a protein's function from mere sequence data are limited, therefore, the general knowledge and skill in the art is not sufficient, thus the specification needs to provide an enabling disclosure. Furthermore, while recombinant and mutagenesis techniques are known in the art, it is not routine in the art to screen

large numbers of mutated proteins where the expectation of obtaining similar activity is unpredictable based on the instant disclosure.

The nature of the invention is protein having pesticidal activity having the sequence set forth in SEQ ID NO:1, however, the claimed invention encompasses an unspecified amount of variants, rendering the invention unpredictable and there is no analogous art. Additionally, the specification does not disclose many methods for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim.

Thus, for all these reasons, the specification is not considered to be enabling for one skilled in the art to make and use the claimed invention.

10. Claims 1, 2, 6, and 9-10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification lacks complete deposit information for the strain of the invention. On page 20 of the instant specification it is disclosed that the strain of the invention was judged to be a novel strain, *Bacillus thuringiensis serovar galleriae* SDS05, deposited at Lab. of Microbial Industry and Technology. The specification does provide the address of the depository or the date the deposit was made. In addition, there is no indication as to whether the deposit was made under the Budapest Treaty or any statements indicating that all restrictions on the availability to the public of these

deposits will be irrevocably removed upon issuance of a patent. Therefore, it is not known whether the information is publicly available or can be reproducibly isolated. Without publicly available deposit information one of skill in the art could not be assured of the ability to practice the invention as claimed.

Applicant's referral to the deposit on page 20 of the specification is noted but is considered insufficient assurance that all of the conditions of 37 CFR 1.801-1.809 have been met. If deposits have not been made under the Budapest Treaty, then in order to certify that the deposits meet the criteria set forth in 37 CFR 1.801-1.809, applicant may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

(A) During the pendency of this application, access to the invention will be afforded to the Commissioner upon request;

(B) All restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

(C) The deposits will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer;

(D) The deposits were viable at the time of deposit;

(E) The deposits will be replaced if they should ever become non-viable.

This requirement is necessary when a deposit is made under the provisions of the Budapest Treaty as the Treaty leaves these specific matters to the discretion of each member State. Amendment of the specification to disclose the date of the deposit and the complete name and address of the depository is required. For further

information concerning deposit practice, applicants attention is directed to *In re Lundak* 773 F 2d 1216 227 USPQ CAFC and 37 CFR 1.801-1.809.

In addition, the claimed invention is directed to a mutant thereof of the above strain and an amino acid sequence having addition, deletion, or substitution of a plurality of amino acids in the amino acid sequence set forth in SEQ ID NO:1 (see claims 2 and 6 for example), and the instant specification does not adequately describe said mutant or variant having the unspecified amount of variations contemplated in claim 2. There are no indicia in the claims or the instant specification as to where in the sequence the variability will occur or if such variability can be tolerated. The specification does not describe any special attributes or features of the claimed mutant or variant. In fact the instant specification simply state that "mutant strains that produce a pesticidal crystal protein may be obtained from the SDS05 strain as an original strain by spontaneous or induced mutation", see for example, page 12. Additionally, the claim recites "transformed microbe", however, mere transformation does not result in protein expression or demonstrate the protein as claimed in hand (see claim 6). With regard to the protein variant (see claim 2), no evidence is provided to demonstrate a protein undergoing the contemplated variations retaining function. Therefore, while it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited, as certain positions in the sequence are critical to the protein's structure/function relationship. Thus, the claims encompass a genus of molecules not adequately described. Note that with the open language "having" which is equivalent to "comprising", the claims encompass any structure that contains a plurality of substitutions, deletions and additions exhibiting a pesticidal activity. Based on the unlimited variations contemplated one skilled in the art

would at best expect a protein that is different or at worst a protein that is not functional. Absent adequate written description of the claimed invention a skilled artisan is being invited to perform undue experimentation. Therefore, for all these reasons the specification lacks adequate written description, and one of skill in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

11. Claim 6 is rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter, which applicant (s) regard as their invention.

Claim 6 lacks antecedent basis for "SDS502 strain and its mutant". It is suggested that the claim is amended to recite "(2-1) *Bacillus thuringiensis serovar galleriae* SDS502, (2-2) a *Bacillus thuringiensis serovar galleriae* mutant and (2-3) a transformed microbe, transformed with a DNA containing a nucleotide sequence encoding a protein having an amino acid sequence described in SEQ ID NO:1 in the Sequence Listing".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claim 2 is rejected under 35 U.S.C. 102 (b) as being anticipated by Payne et al. (U.S. Patent No. 5,262,158, November 16,1993) based on a protein sequence derived by addition, deletion or substitution of a plurality of amino acids having SEQ ID NO:1.

Payne et al. disclose a protein comprising the sequence set forth in SEQ ID NO: 1 of the instant application with a 66.3%% sequence identity. The protein taught by the reference is a *Bacillus thuringiensis* isolate for controlling Acarides pests. Therefore, the limitation of the claim is met by the reference as the same organism is disclosed and a sequence obtained from this organism that fits in the recited "protein sequence derived by addition, deletion or substitution of a plurality of amino acids having SEQ ID NO:1, having pesiticidal activity". Although, the isolate taught by the reference is for example, PS86A1 and not SDS502, as the claim does not describe where in the sequence the variability will occur or how much variability will occur or recite the specific strain, this reference is encompassed by the breath of the claim and anticipates the claimed limitations. Therefore, the limitation of the claim is met by this reference (see sequence alignment and abstract).

Conclusion

13. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope A. Robinson whose telephone number is 571-272-0957. The examiner can normally be reached on Monday-Friday from 9:00 a.m. to 6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher S.F. Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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